(2) identifying enzymatic activities associated within said gene-containing DNA sequence;

(3) introducing one or more specified changes into said gene-cotnaining DNA sequence which codes for one of said enzymatic activities resulting in an altered DNA sequence;

(4) introducing said altered DNA sequence into a polyketide-producing microorganism to replace the original sequence;

(5) growing a culture of the altered microorganism under conditions suitable for the formation of the specific macrolide polyketide analog; and

(6) isolating said specific macrolide polyketide analog from the culture, wherein said polyketide biosynthetic gene-containing DNA sequence comprises genes which encode the enzymatic activities comprising a polyketide synthase.

58. The method of claim 57 wherein said polyketide synthase enzymatic activities comprise β-ketoreductase, dehydratase, acyl carrier protein, enoylreductase, β-ketoacyl ACP synthase, and acyltransferase.

59. The method of claim 57 wherein said alteration which occurs in the DNA sequence results in the inactivation of one or more enzymatic activities involved in the processing of the β-carbonyl of said polyketide.

60. The method of claim 59 wherein said inactivated enzymatic activities affecting the processing of the β-carbonyl of said polyketide comprise β-ketoreductase, dehydratase, and enoylreductase.

61. The method of claim 59 wherein said alteration in the DNA sequence results in the addition of one or more enzymatic activities involved in the β-carbonyl processing of said polyketide.

62. The method of claim 61 wherein said additional enzymatic activities are selected from the group consisting of β-ketoreductase, β-ketoreductase and dehydratase, and β-ketoreductase, dehydratase and enoylreductase.

63. The method of claim 57 wherein said alteration occurring in the DNA segment results in the inactivation of one or more enzymatic activities involved in the condensation of carbon units to the nascent polyketide structure.

A1 cont.

64. The method of claim 63 wherein said enzymatic activities affecting the condensation of carbon units to the nascent poyketide structure comprise β-ketoacyl ACP synthase, acyl carrier protein, and acyltransferase.

65. The method of claim 57 wherein said alteration in the DNA sequence results in a change in the length of the polyketide synthesized.

66. The method of claim 65 wherein said alteration results in the increase of the length of the polyketide.

67. The method of claim 66 wherein said alteration comprises the addition of DNA sequences encoding the enzymatic activities consisting of acyltransferase, acyl carrier protein and β-ketoacyl ACP synthase.

68. The method of claim 65 wherein said alteration results in the decrease of the length of the polyketide.

69. The method of claim 68 wherein said alteration consists of the deletion of a DNA segment between two sequences encoding corresponding enzymatic activities.

70. The method of claim 69 wherein said corresponding enzymatic activities are selected from the group consisting of β-ketoreductases, dehydratases, acyl carrier proteins, enoylreductases, β-ketoacyl ACP synthases, and acyltransferases.

71. The method of claim 57 wherein said alteration consists of the replacement of the DNA segment encoding an acyltransferase with a DNA segment encoding an acyltransferase of different specificity.

A1 cont.

72. The method of claim 57 wherein said DNA sequence is isolated from a species from the *Actinomycetales* family.

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73. The method of claim 72 wherein said DNA sequence is isolated from a genus selected from the group consisitng of *Actinomyces, Dactylosporangium, Micromonospora, Nocardia, Saccharopolyspora, Streptoverticillium, and Streptomyces.*

74. The method of claim 73 wherein said genus is selected from the group consisting of *Saccharopolyspora and Streptomyces.*

75. The method of claim 74 wherein said genus is *Saccharopolyspora* and the species is *erythraea.*

76. The method of claim 74 wherein said genus is *Saccharopolyspora* and the species is *hydroscopicus.*

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77. The method of claim 57 wherein said polyketide is selected from the group consiting of macrolides, tetracyclines, polyethers, polyenes, ansamycins and derivatives or analogs thereof.

78. The method of claim 77 wherein said polyketide is a macrolide.

79. The method of claim 78 wherein said macrolide is an erythromycin.

80. The method of claim 79 wherein said erythromycin analog is selected from the group consisting of 11-oxo-11-deoxyerythromycin A, 7-hydroxyerythromycin A, 6-deoxy-7-hydroxyerythromycin A, 7-oxoerythromycin A, 3-oxo-3-deoxy-5-desosaminylerythronolide A, Δ-6,7-anhydroerythromycin A, ((14S, 15S)14(1-hydroxyethyl)erythromycin A, 11-epifluoro-15-norerythromycin A, 14-(1-propyl)erythromcyin A, and 14[1(1-hydroxypropyl)]erythromycin A.

A1 cont.

81. The method of claim 57 wherein said DNA sequence, designated *eryA*, encodes the enzymatic activities associated with the formation of 6-deoxyerythronolide B.

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82. The method of claim 57 wherein said gene-containing DNA sequence encodes one or more enzymatic activities in the rapamycin biosynthetic pathway.

83. The method of claim 23 wherein said macrolide is a rapamycin analog.--

**IN THE SPECIFICATION**

On page 1, immediately below the title, please insert the following application history: --This application is a continuation application of U.S. Serial No. 08/997,467, filed December 23, 1997, now ~~allowed~~ U.S. Patent No. 6,200,813, which is a divisional of U.S. Serial Number 08/858,003, filed May 16, 1997, now U.S. Patent No. 6,060,234, which is a continuation-in-part of U.S. Serial No. 08/642,734, filed January 17, 1991, now abandoned, all of which are incorporated herein by reference in their entirety.--

wow 5/23/03

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**Remarks**

This preliminary amendment accompanies a Request for Continuation Application filed pursuant to 37 CFR §1.53. In the amendments shown above, Applicants have cancelled, without prejudice, claims 1-56. Applicants have added new claims 57-83. Applicants respectfully submit that new claims 57-83 find support in the